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Letter to the Editor

Erythema Nodosum Secondary to Granulocyte Colony-Stimulating Factor in a Patient with Hodgkin Lymphoma during CD34$^+$ Cell Mobilization for Autologous Peripheral Blood Stem Cell Transplantation: A Dose-Mediated Effect

Stem cell mobilization techniques incorporate granulocyte colony-stimulating factor (G-CSF) alone, in combination with chemotherapy, or with other cytokines. A variety of cutaneous disorders have been described with G-CSF, including Sweet's syndrome, pyoderma gangrenosum, and necrotizing vasculitis. Erythema nodosum (EN) is a rarely described cutaneous disorder related to G-CSF administration.

A 28-year-old man with nodular sclerosing Hodgkin lymphoma was initially diagnosed with advanced disease. He did not attain a complete remission with doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD). Salvage therapies consisted of gemcitabine-vinorelbine and etoposide, methylprednisolone, cytarabine, and cisplatin (ESHAP). He presented to our service for an autologous peripheral blood stem cell transplantation. In the event that the patient required tandem transplantation, we aimed to harvest a total of 10×10^6 CD34$^+$ cells per kilogram. Mobilization 1 consisted of G-CSF 12 μg/kg/d × 5 days, which yielded 4.68×10^6 CD34$^+$ cells per kilogram. Mobilization 2 consisted of ifosfamide, carboplatin, and etoposide (ICE) plus G-CSF (12 μg/kg/d). This procedure was complicated by a catheter-related infection, and the harvest was stopped. Mobilization 3 was identical to mobilization 1 (G-CSF 12 μg/kg/d × 5 days) and yielded 6.2×10^6 CD34$^+$ cells per kilogram.

After completion of mobilization 3, the patient complained of multiple painful bilateral lower extremity lesions. The patient also reported similar lesions after the first stem cell mobilization but had neglected to inform his physicians. Physical examination revealed multiple indurated, erythematous plaques on the shins and posterior calves bilaterally, with the largest measuring 5 × 4 cm.

Dermatology was consulted, and a diagnosis of G-CSF–induced EN was rendered. A skin biopsy was not performed because of the typical clinical findings associated with EN. The patient was treated with nonsteroidal anti-inflammatory drugs, ice, and bed rest, and the lesions resolved within 3 days of cessation of G-CSF. Subsequent treatment with a lower dose of G-CSF (5 μg/kg/d) after transplantation did not result in any further cutaneous findings.

Various skin disorders have been reported after the administration of G-CSF. Although there are several reported cases of G-CSF–induced Sweet's syndrome, our literature review revealed 3 case reports of panniculitis, such as EN, associated with G-CSF administration [1-3]. EN is most often related to underlying infectious etiologies, but it has been uncommonly associated with malignancies such as Hodgkin lymphoma [4].

Both Sweet's syndrome and EN are marked by an inflammatory infiltrate without an associated vasculitis. However, there are clear clinical differences between the 2 disorders that can allow diagnosis on the basis of physical examination. Sweet's syndrome usually presents as papules or vesicles that reflect its dermal involvement, whereas EN classically involves nodules/plaques. In addition, Sweet's syndrome most often involves the face, neck, and upper extremities, whereas EN usually involves the pretibial areas [5]. If the diagnosis of EN or Sweet's syndrome is unclear, a biopsy should be undertaken, because the lesions with Sweet's syndrome may require steroid administration.

To our knowledge, this is the first reported case of EN in a patient undergoing stem cell mobilization with G-CSF. Our case adds credence to a dose-mediated effect for G-CSF–induced skin lesions [1]. Typically the lesions resolve after cessation of G-CSF, and resolution can be related to increasing doses of the drug. The pathogenesis of these lesions remains unclear but may be related to the cellular environment created with an increase in neutrophils. It has been hypothesized that these lesions may be caused by a neutrophil recovery syndrome in which an increase in

neutrophils, either spontaneous or drug-induced, may lead to cytokine release and upregulation of certain adhesion molecules that culminates in accumulation of neutrophils in the dermis [6]. It is clear that there must be a high clinical suspicion of cutaneous involvement with G-CSF administration given the wide variety of skin disorders, including EN, associated with the drug.

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